AMENDMENTS TO THE CLAIMS

Please amend claims 1, 4-7, 10-13, and 16-26, and cancel claims 14 and 15, as set forth below. Withdraw claims 27-30 without prejudice or disclaimer.

The current listing of claims replaces all prior listings.

1. (Currently Amended) A method comprising:

a) immobilizing one or more unlabeled nucleic acid molecules to a surface;

b) sequentially releasing the ~~using an exonuclease to release~~ unlabeled nucleotides from one end of one or more of the immobilized unlabeled nucleic acid molecules with an exonuclease;

c) separating the released nucleotides from the exonuclease and the one or more nucleic acid molecules;

d) identifying the released unlabeled nucleotides in a buffer comprising an alkali-metal halide salt by Raman spectroscopy; and

e) determining the sequence of the nucleic acid from the identified nucleotides.

2. (Original) The method of claim 1, wherein single molecules of unlabeled nucleotides are identified by Raman spectroscopy.

3. (Original) The method of claim 2, wherein a single nucleic acid molecule is sequenced.

4. (Currently Amended) The method of claim 1, wherein multiple nucleic acid molecules of the same sequence or multiple nucleic acid molecules of different sequences are sequenced simultaneously.

5. (Currently Amended) The method of claim 1, wherein the one or more nucleic acid molecules are [is] immobilized ~~attached~~ to [a] the surface via covalent attachment.

6. (Currently Amended) The method of claim 1, wherein the released nucleotides are identified

by surface enhanced Raman spectroscopy (SERS), surface enhanced resonance Raman spectroscopy (SERRS) and/or coherent anti-Stokes Raman spectroscopy (CARS).

7. (Currently Amended) A method comprising:

a) obtaining nucleotides covalently linked to gold or silver, or gold or silver nanoparticle(s), wherein the nucleotide and nanoparticles are linked via a terminal reactive cross-linking group, selected from the group consisting of epoxide groups, azido groups, triazine groups, arylazido groups and diazo groups;

b) synthesizing one or more nucleic acid molecules comprising the gold or silver, or gold or silver nanoparticles;

c) immobilizing the nucleic acid molecule of step (b) on a solid substrate;

d) sequentially releasing ~~removing~~ nucleotides from one end of one or more nucleic acid molecules via an exonuclease;

~~attaching each nucleotide to at least one nanoparticle~~;

e) identifying the released unlabeled nucleotides in a buffer comprising an alkali-metal halide salt by Raman spectroscopy; and

f) determining the sequence of the nucleic acid molecule.

8. (Original) The method of claim 7, wherein single molecules of nucleotides are identified by Raman spectroscopy.

9. (Original) The method of claim 8, wherein a single nucleic acid molecule is sequenced.

10. (Currently Amended) The method of claim 7, wherein multiple nucleic acid molecules of the same sequence or multiple nucleic acid molecules of different sequences are sequenced simultaneously ~~the nucleotides are unlabeled~~.

11. (Currently Amended) The method of claim 7, wherein the alkali-metal halide salt is selected from the group consisting of MgCl, CaCl, NaF, KBr, LiI, and LiCl ~~the nanoparticles are~~

~~modified with one or more linker compounds~~.

12. (Currently Amended) The method of claim 11, wherein the alkali-metal halide salt is LiCl ~~the nucleotides are covalently attached to the linker compounds~~.

13. The method of claim [12] 7, wherein the linker compound is 3-glycidoxypropyltrimethoxysilane (GOP).

14. (Canceled)

15. (Canceled)

16. (Currently Amended) The method of claim 1[5], wherein nanoparticles are attached to the 3' end of the nucleic acid.

17. (Currently Amended) The method of claim 7, wherein [said] the released nucleotides are identified by surface enhanced Raman spectroscopy (SERS), surface enhanced resonance Raman spectroscopy (SERRS) and/or coherent anti-Stokes Raman spectroscopy (CARS).

18. (Currently Amended) The method of claim 7, further comprising separating the nucleotides from the one or more nucleic acid molecules by transferring the released nucleotides through a microfluidic channel.

19. (Currently Amended) The method of claim [7] 18, wherein microfluidic channel is a metal coated channel ~~an exonuclease is used to remove the nucleotides from said nucleic acid~~.

20. (Currently Amended) The method of claim 19[6], wherein the metal is silver, gold, platinum, copper, or aluminum ~~nucleotides are removed by acid hydrolysis~~.

21. (Currently Amended) The method of claim 20, wherein the nanoparticle and microfluidic channel comprise silver ~~further comprising using acid hydrolysis to remove the purine or pyrimidine base from the nucleotide~~.

22. (Currently Amended) A method comprising:

a) obtaining pyrimidine nucleotides that are attached to Raman labels;

b) synthesizing a nucleic acid molecule comprising the labeled nucleotides;

c) removing nucleotides from one end of the nucleic acid;

d) identifying the released nucleotides in a buffer comprising an alkali-metal halide salt by Raman spectroscopy; and

e) determining the sequence of the nucleic acid molecule.

23. (Currently Amended) The method of claim 22, wherein the alkali-metal halide salt is selected from the group consisting of MgCl, CaCl, NaF, KBr, LiI, and LiCl ~~single nucleotide molecules are identified by Raman spectroscopy.~~

24. (Currently Amended) The method of claim 22, wherein the alkali-metal halide salt is LiCl ~~each type of nucleotide is labeled with a distinguishable Raman l~~abel.

25. (Currently Amended) The method of claim 22, wherein multiple nucleic acid molecules of the same sequence or multiple nucleic acid molecules of different sequences are sequenced simultaneously ~~only pyrimidine nucleotides are labeled with Raman labels.~~

26. (Currently Amended) The method of claim 22, further comprising:

(i) obtaining at least one template nucleic acid molecule;

(ii) hybridizing the template nucleic acid molecule to a primer; and

(iii) adding a DNA polymerase to synthesize [said] the nucleic acid molecule.

27. (Withdrawn) An apparatus comprising:

a) a reaction chamber;

b) a microfluidic channel in fluid communication with the reaction chamber;

c) a flow-through cell in fluid communication with the microfluidic channel; and

d) a Raman detection unit operably coupled to the flow-through cell.

28. (Withdrawn) The apparatus of claim 27, wherein the Raman detector is capable of detecting single molecules of nucleotides.

29. (Withdrawn) The apparatus of claim 28, wherein the nucleotides are unlabeled.

30. (Withdrawn) The apparatus of claim 27, further comprising nanoparticles in the flow-through cell.